UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/554,308	04/17/2006	Fumio Takaiwa	201487/1160	1884

7590 09/24/2009

Michael L Goldman
Nixon Peabody
Clinton Square
P O Box 31051
Rochester, NY 14603-1051

EXAMINER	
WORLEY, CATHY KINGDON	

ART UNIT	PAPER NUMBER
1638	

MAIL DATE	DELIVERY MODE
09/24/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/554,308	TAKAIWA ET AL.	
	Examiner	Art Unit	
	CATHY K. WORLEY	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 June 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8,11-19,21-29,34-43 and 46-48* is/are pending in the application.

4a) Of the above claim(s) *1-3,11-19,22-25,34-40,42,43 and 46-48* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4-8,21,26-29 and 41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/8/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The amendment filed June 8, 2009, has been entered.

2. Claims 9, 10, 20, 30-33, 44, and 45 have been cancelled.

Claims 1-8, 11-19, 21-29, 34-43, and 46-48 are pending.

Claims 1-3, 11-19, 22-25, 34-40, 42, 43, and 46-48 are withdrawn.

3. Claims 4-8, 21, 26-29, and 41 are examined in the present office action.

4. This application contains claims 1-3, 11-19, 22-25, 34-40, 42, 43, and 46-48, drawn to inventions nonelected with traverse in the response filed Feb. 27, 2008. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144). See MPEP § 821.01.

Priority

5. Acknowledgment is made of applicant's claim for foreign priority based on an application filed in Japan on April 24, 2003. The Examiner has obtained the certified document from the PCT office, and the Applicant has provided a

translation, therefore, the instant application is given the priority date of April 24, 2003.

Objections and Rejections that are Withdrawn

6. The objection to claims 4 and 41 for depending from withdrawn claims of non-elected inventions is withdrawn in light of the Applicant's amendments to the claims.

7. The objections to claims 9, 10, 20, 30-33, 44, and 45 for failing to further limit the parent claims are withdrawn in light of the Applicant's cancellation of these claims.

8. The rejection of claim 21 under 35 USC 112, second paragraph, is withdrawn in light of the Applicant's amendments to the claims, however, it is replaced with a new objection due to awkward wording (see below).

9. The rejections of claims 9, 10, 20, 30-33, 44, and 45 under 35 USC 103(a) are withdrawn in light of the Applicant's cancellation of these claims

Claim Objections

10. Claims 4 and 21 are objected to because of the following informalities:

- In claim 4, the recitation in part (a) of "and/or a DNA encoding an ER-retention signal sequence is added to the 3'-end thereof;" renders this part of the claim inclusive of a DNA construct that has an ER-retention signal sequence but does not have a signal sequence. This would not be directed to the ER, so it is technically incorrect. A polypeptide can not be retained in the ER if it is not directed to the ER with a signal sequence in the first place. The recitation in part (b) has the same issue. The Applicant is advised to replace "and/or" with - - and, optionally, - - , in parts (a) and (b) of claim 4.
- In claim 21, it is technically/grammatically incorrect. The recitation that a plant comprises a rice plant is awkward and incorrect. A plant can be a rice plant, but it can not "comprise" a rice plant. The Applicant is advised to replace "comprises" with - - is - -.

Appropriate correction is requested. It is noted that these new objections were necessitated by the Applicant's amendments to the claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. Claims 4, 5, 7, 8, 21, 26, 28, 32, and 41 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Alli et al (Phytochemistry Reviews (2002) Vol. 1; pp. 55-66) in view of Hirahara et al (J. Allergy Clin. Immunol. (2001) Vol. 108; pp. 94-100). The Applicant's arguments in the response filed on June 8, 2009, have been fully considered but were not found to be persuasive.

The claims are directed to a method for accumulating an allergen-specific T-cell epitope in an edible part of a plant by introducing a DNA comprising a storage protein promoter operably linked to a DNA encoding a storage protein signal sequence and an allergen-specific T-cell epitope.

Because the recitations of an ER-retention signal are optional (due to "and/or" language), an ER-retention signal is not required. This is a well-known tool for expression of recombinant proteins, therefore, the Examiner takes official notice that if the claims are amended to require it, adding an ER-retention signal would be obvious over the prior art.

Alli et al teach the production of vaccines for oral delivery of antigens (see entire article). They teach that plant-based edible vaccines may provide an attractive, safe, and inexpensive alternative to conventional vaccine production (see abstract). They teach that several different antigens have been successfully produced in plants (see last paragraph on page 56); and they specifically teach the

production of a viral glycoprotein in rice seeds using the glutelin (Gt3) promoter and the Gt3 signal peptide (see page 61, Figure 3).

Alli et al do not teach an allergen-specific T-cell epitope.

Hirahara et al teach the production of recombinant peptides that are allergen-specific T-cell epitopes from the Cry j 1 and Cry j 2 proteins from Japanese cedar pollen (see entire article).

At the time the invention was made, it would have been obvious and within the scope of one of ordinary skill in the art to modify the method taught by Alli et al to express the Cry j 1 or Cry j 2 epitopes that are taught by Hirahara et al. One would have been motivated to do so because Alli et al teach that their method can be useful for the production of any edible vaccine and Hirahara et al teach that the Cry j 1 and Cry j 2 peptides were effective for producing positive T-cell responses in more than 90% of the volunteers tested (see page 99). Furthermore, Hirahara et al teach that peptide based allergen immunotherapy is a new approach to treating allergen-specific T cells, and they teach that Japanese cedar pollinosis is one of the most common seasonal allergic disease in Japan with more than 10% of the population being affected (see page 94) and this demonstrates that there would be a need for immunotherapy directed toward Japanese cedar pollinosis. Given the success of utilizing Cry j 1 and Cry j 2 peptides for immunotherapy that was taught by Hirahara et al and given the successes in producing edible vaccines in plant seeds as taught by Alli et al, one would have had a reasonable expectation of

success in producing Cry j 1 and Cry j 2 peptides in rice seeds utilizing the Gt3 promoter and signal peptide.

The Applicant argues that the proposed combination of Alli and Hirahara is rife with unpredictability, undermining any reasonable expectation of success (see paragraph bridging pages 9-10 of the response filed on June 8, 2009). The Applicant argues that prior to the present invention, there were no reports of high accumulation (3-4% of total proteins, 50 μg per one rice grain) of an artificial hybrid peptide with sequentially linked T cell epitopes; and therefore high accumulation can not be predicted from the prior art (see second paragraph on page 10 of the response). This is not persuasive, however, because the instant claims do not require any particular amount of accumulation. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., 3-4% of total proteins, 50 μg per one rice grain, or "high accumulation") are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

The Applicant argues that they have an unexpectedly improved property because the claimed rice seeds can be heated for 20 minutes of cooking, and there is no alteration in the T-cell epitope-linked peptide (see paragraph bridging pages 10-11 and see second paragraph on page 11 of the response). This is not persuasive,

however, because it is known in the art that T-cell epitopes are small linear peptides with no important tertiary structure; therefore, the fact that they can be cooked without altering the peptides is not a surprising or unexpected result. See the teachings of Davis et al (Allergy (1998) Vol. 53 - Suppl.; pp. 102-105) who teach that "heating destroys most conformational epitopes by unfolding native proteins, leaving only the linear epitopes" (see last paragraph in right column on page 103). Taken together with the teachings of Hirahara et al that the Cryj1 and Cryj2 T-cell antigens were small peptides (see page 96, Figure 1) and with the general knowledge in the art that T-cell epitopes are short linear peptides, it is not a surprising result that a T-cell epitope can be heated without destroying its antigenicity.

12. Claims 6, 27, and 29 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Alli et al (Phytochemistry Reviews (2002) Vol. 1; pp. 55-66) in view of Hirahara et al (J. Allergy Clin. Immunol. (2001) Vol. 108; pp. 94-100) as applied to claims 4, 5, 7-10, 20, 21, 26, 28, 30, 32, 41, and 44 , above, and further in view of Bagga et al (US Patent No. 5,990,384; issued on Nov. 23, 1999) and further in view of Kim et al (Protein Engineering (1990) Vol. 3; pp. 725-731). The Applicant's arguments in the response filed on June 8, 2009, have been fully considered but were not found to be persuasive.

The claims are directed to a method for accumulating an allergen-specific T-cell epitope in a plant by introducing a DNA comprising a storage protein promoter operably linked to a DNA encoding a polypeptide in which an allergen-specific T-cell epitope is inserted into a variable region of a storage protein.

Alli et al in view of Hirahara et al teach a method for accumulating an allergen-specific T-cell epitope in a plant by introducing a DNA comprising a storage protein promoter operably linked to a DNA encoding a storage protein signal peptide and an allergen-specific T-cell epitope; as discussed above in the rejection under 35 USC 103 of claims 4, 5, 7-10, 20, 21, 26, 28, 30, 32, 41, and 44.

Alli et al in view of Hirahara et al do not teach a polypeptide in which an epitope is inserted into a variable region of a storage protein.

Bagga et al teach a stable protein that is expressed in a plant as a fusion protein comprising a zein protein (which is a storage protein) and an operably linked protein or peptide (see abstract).

Kim et al teach that modifications of glycinin (which is a storage protein) can be rationally designed by identifying the variable domains and making insertions in the cDNA regions corresponding to variable domains (see abstract).

At the time the invention was made, it would have been obvious and within the scope of one of ordinary skill in the art to combine the teachings of Alli et al, Hirahara et al, Bagga et al, and Kim et al to arrive at a method of expressing a Cry j epitope as a fusion with a storage protein by inserting the Cry j peptide into a

variable region of a storage protein. Bagga et al teach that heterologous proteins, such as antigens, can be expressed in plants transformed with the storage proteins which can act as a carrier protein such that the fusion protein will coalesce and accumulated in the cell as a protein body (see paragraph bridging columns 5 and 6). Therefore, one would have been motivated to use storage proteins, such as zeins, as carriers for the antigenic cry j peptides. The teachings of Kim et al would have motivated one of ordinary skill in the art to insert the peptide into a variable region of the storage protein. Given the success of utilizing Cry j 1 and Cry j 2 peptides for immunotherapy that was taught by Hirahara et al and given the successes in producing edible vaccines in plant seeds as taught by Alli et al, one would have had a reasonable expectation of success in producing Cry j 1 and Cry j 2 peptides in rice seeds utilizing the Gt3 promoter and signal peptide. Given the success in producing zeins that accumulate to high levels that is taught by Bagga et al and given the success of inserting peptides into the variable regions of a storage protein that is taught by Kim et al, one would have had a reasonable expectation of success in producing fusion proteins comprising Cry j peptides inserted into variable regions of a storage protein.

The Applicant argues that no one had introduced a 100-200 amino acid residue peptide and managed to successfully and stably accumulate such a long peptide (see third paragraph on page 12 of the response). This is not persuasive, however, because the instant claims are directed to expression of a T-cell epitope

antigen which is not a long 100-200 amino acid residue peptide. None of the claims require a 100-200 amino acid residue peptide, therefore this is arguing a limitation that does not appear in the claims.

13. No claim is allowed.

14 **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

15 Any inquiry concerning this communication or earlier communications from the examiner should be directed to CATHY K. WORLEY whose telephone number is (571)272-8784. The examiner is on a variable schedule but can normally be reached

on M-F 10:00 - 4:00, with additional variable hours before 10:00 and after 4:00 with additional variable hours before 10:00 and after 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg, can be reached on (571) 272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Cathy K. Worley/
Primary Examiner, Art Unit 1638